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8EHQ-92-12509
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INIT

September 15, 1992

Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Sir or Madam:

Subject: Report submitted in accordance with guidelines established by the U. S. Environmental Protection Agency Registration and Agreement for the TSCA 8(e) Compliance Audit Program

Report submitted by: Eastman Kodak Company
343 State Street
Rochester, NY 14650
(716) 724-4000
CAP Agreement Identification Number (8ECAP-0039)

The report pertains to N,N'-methanetetraylbiscyclohexanamine (synonym: dicyclohexylcarbodiimide) [CAS # 538-75-0] and is being submitted because of effects observed in a series of acute toxicity tests conducted by multiple routes of exposure. The test material was a moderate skin irritant in an acute dermal toxicity study in guinea pigs and a severe eye irritant in a study conducted in a single rabbit. The dermal LD_{50} was reported to be as low as 1-5 drops in guinea pigs. The inhalation LC_{50} was 0.159-0.417 mg/L in rats. Histologic changes were seen in some tissues following inhalation exposure. The significance of these changes is unclear, because of the small numbers of animals examined and the lack of equivalent control animals. Dicyclohexylcarbodiimide was a skin sensitizer of low activity in 2 of 5 animals tested. At least five cases of dermal sensitization have occurred in manufacturing employees due to exposure to this material. Details are not available for these cases. The report is being identified as a study involving other than human effects (Unit II.B.2.b of CAP Agreement).

Annual sales of this chemical have been 26-180 kg/year.

mm
2/9/95

INHALATION CHEMICAL: Dicyclohexyl carbodiimide

KP# 54295

Chemical Formula Type of Exposure	Animals* No. and Species	Conc.	Time	Mortality	Symptoms
3 1/2 L/min. through a gas washing bottle heated in a water bath at 50°C. Chamber temperature, 25°C.	3 R	0.159 mg/L 18.9 ppm	6 hours	0/3 1/3 in 48 hrs.	Pilo-erection, lacrimation - 5 min. Vasodilation - 5 minutes 14 day wts. 1 + (34. gm) 1 - (13 gm)
2 L/min. through a gas washing bottle heated in a water bath at 70°C. Chamber temperature, 25°C.	3 R	0.417 mg/L 49.5 ppm	6 hours	0/3 3/3 in 48 hrs.	Pilo-erection - 5 minutes Lacrimation - 10 minutes Vasodilation - 15 minutes
2 L/min. through a gas washing bottle heated in a water bath at 100°C. Chamber temperature, 25.5°C.	3 R	1.32 mg/L 156.7 ppm	6 hours	0/3 1/3 in 24 hrs.	Pilo-erection - 5 minutes Blinking, lacrimation - 10 min. Vasodilation - 15 minutes Dyspnea - 6 hours 1 Rat sacrificed in 22 hours 14 day wt. 1 - (79. gm)

65-510

* G.P. - Guinea Pig, M - Mouse,
R - Rat, RB - Rabbit

Dicyclohexyl carbodiimide

65-510

The lungs of rats exposed to 18.9 ppm all showed acute and chronic inflammatory reactions. This was true of those sacrificed at 14 days as well as the one that died 48 hours after exposure. The rat dying in 48 hours exhibited acute inflammation in both the trachea and stomach. The stomach contained foci of necrosis and the liver was necrotic. 1/2 rats sacrificed at 14 days showed a mild generalized testicular atrophy.

Rats exposed to 156 ppm showed the pulmonary inflammation as noted above and in addition, 2/3 showed edema 24 hours after exposure. The one 14-day survivor had 10% of its lung consolidated and had atrophic testes.

TOXICITY REPORT - E.K.CO. - LABORATORY OF INDUSTRIAL MEDICINE

Chemical: Dicyclohexyl Carbodiimide

Solution	Animals* No. and Species	Route**	Dose Range	Approx. LD_{50}	Symptoms	Time of Death	Wt. Change 2 wks
Acute Toxicity			mg/kg	mg/kg			
Undilute - heated to melt	10R	PO	200-3200	400	Slight to quite weak, rough coat, sides caved in, diarrhea.	5 hrs.-5 days	3+
Undilute - 10% + 1% in corn oil	31R	IP	2.5-3200	10-25	Slight to moderate weakness, after 24 hrs. abdominal distention, tremor, not eating, labored respirations, cyanosis.	1/2 hr-3 days	6+
10% in corn oil	6M	PO	200-800	>800	Normal to moderate weakness, rough coat.	-	6+
10% + 1% in corn oil	16M	IP	1-100	25 (1%	Slight to moderate weakness, rough coat.	2-5 days	5+
					Notebook No.	62 P	600
Skin Absorption and Irritation			cc/kg	cc/kg			
					Moderate to gross edema, #3 erythema or hemorrhagic.		+26
Undiluted	2 G.P.	Cuff	1.0-10.0	>10.0	Eschar over entire patch at 1 week.	-	-12
					2° eschar, heavy scarring, no hair or heavy black eschar at 2 weeks.		
					Notebook No.	62 P	600

*G.P. - Guinea Pig, M - Mouse, R - Rat, RB - Rabbit

**PO - Orally, IP - Intraperitoneally, IM - Intramuscularly, IC - Intracutaneously

6-14-63

Remarks: Slightly toxic orally in mice, moderately toxic PO in rats. Highly toxic IP.
Moderate skin irritant, may be absorbed.
Irritating to the eye causing transient corneal opacity. Apparently damaged eyelids permanently.

Chemical: Dicyclohexyl carbodiimide

SKIN ABSORPTION AND IRRITATION

Chemical	Formula	Animals* No. and Species	Route	Dose Range cc/kg	Approx. LD_{50} cc/kg	Symptoms	Time of Death	Wt. Change 2 wks
		9 GP	Drop on	10 drops 5 drops 1 drop	1-5 drops	24 hrs: to 4 erythema, to 2 edema 1 wk: to 3 erythema or eschar covering dropped on area 2 wks: to 2 erythema with 2o eschars over entire dropped on area	< 24 hrs < 24 hrs < 24 hrs < 24 hrs < 24 hrs 96 hrs 48 hrs	+ 49 - 8
Moderate skin irritant - absorbed through skin								

* G.P. - Guinea Pig, M - Mouse,
R - Rat, RB - Rabbit

A - Acetone, D - Dioxane, CO - Corn oil, O - Olive oil
P.G. - Propylene glycol

SKIN ABSORPTION AND IRRITATION Chemical: Dicyclohexylcarbodiimide

Chemical	Formula	Animals* No. and Species	Route	Dose Range cc/kg	Approx. LD_{50} cc/kg	Symptoms	Time of Death	Wt. Change 2 wks
		3 G.P.	Drop on		<0.1 ml	>24 hr.: Found dead at 8:00 a.m., 2-3 ery.	<1 day	
		3 G.P.	Cuff	5.0-20.0	5-10	24 hr.: To severe gross edema and patch hemorrhagic and some necrosis. 1 wk.: Mod. edema, thin eschar over entire patch with 3 ery. at periphery. 2 wk.: Eschars - some 2°, heavy scarring and complete alopecia.	3 days	+19

Remarks: Strong skin irritant. May be absorbed through skin.

69-286

* G.P. - Guinea Pig, M - Mouse, R - Rat, RB - Rabbit

A - Acetone, D - Dioxane, CO - Corn oil, O - Olive oil
P.G. - Propylene glycol

10-21-69/bb

TOXICITY REPORT - E.K.CO. - LABORATORY OF INDUSTRIAL MEDICINE

Chemical: Dicyclohexylcarbodiimide

Solution	Animals* No. and Species	Route**	Dose Range	Approx. LD_{50}	Symptoms	Time of Death	Wt. Change 2 wks
Acute Toxicity			mg/kg	mg/kg			
					Notebook No.	P	
Skin Absorption and Irritation			cc/kg	cc/kg			
Undilute	1 G.P.	Drop on		0.05 ml	24 hr.: Severe ery., mod. edema. 48 hr.: Severe ery., mod. edema. 1 wk.: Mod. ery., no edema. 2 wk.: Sl. ery. and complete alopecia.	-	+30
					Notebook No.	69 p	286

*G.P. - Guinea Pig, M - Mouse, R - Rat, RB - Rabbit

**PO - Orally, IP - Intraperintoneally, IM - Intramuscularly, IC - Intracutaneously

11-14-69/bb

Remarks: Strong skin irritant.

TOXICITY REPORT - E. K. CO. - LABORATORY OF INDUSTRIAL MEDICINE

Chemical: Dicyclohexyl carbodiimide

Solution	Animals* No. and Species	Type of Test	Initial Score 24 hrs	Initial Score 48 hrs	Final Score 24 hrs	Final Score 48 hrs
Skin Sensitization						
1% in A + D + GP fat	5 GP	Drop on	3.0	3.2	-	-
0.1% for initial & shoulder drop on; 1% for sensitization drop on	5 GP	Drop on	1.8	1.6	1.9	1.8
Solvent control	4 GP	Drop on	1.0	1.0	1.0	1.0
Phenylhydrazine	4 GP	Drop on	1.4	1.4	4.4	4.2

Notebook No. 65 P 510

Solution	Animals* No. and Species	Route**	Dose Range mg/kg	Approx. LD_{50} mg/kg	Symptoms	Time of Death	Wt. Change 2 wks
Chronic Toxicity							

Notebook No. ___ P ___

Type of Exposure	Animals* No. and Species	Conc.	Time	Mortality	Symptoms
Inhalation					

Notebook No. ___ P ___

*G.P. - Guinea Pig, M - Mouse
R - Rat, RB - Rabbit

**PO - Orally, IP - Intraperitoneally,
IM - Intramuscularly, IC - Intracutaneously

Remarks:

Sensitizing of low activity to 2/5 GP

Chemical: Dicyclohexyl Carbodiimide

SKIN ABSORPTION AND IRRITATION

Chemical Formula	Animals* No. and Species	Route	Dose Range cc/kg	Approx. LD_{50} cc/kg	Symptoms	Time of Death	Wt. Change 2 wks
EYE DAMAGE:				Initial	Slight blinking.		
Dry chemical	RB	Eye	several crystals	one hour	Slight to moderate erythema of lids, nictitating membrane, palpebra, conjunctiva, and upper orbital conjunctiva.		
				24 hrs.	Slight increase of erythema, cornea stained.		
				48 hrs.	Moderate erythema with slight edema, iris injected.		
				14 days	Conjunctive - OK Lids - thickened - perhaps scar tissue. Cornea and nictitating membrane - OK Defoliation around eye.		
					Notebook No.	62 P.	600

* G.P. - Guinea Pig, M - Mouse,
R - Rat, RB - Rabbit

A - Acetone, D - Dioxane, CO - Corn oil, O - Olive oil
P.G. - Propylene glycol

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D. C. 20460

R. Hays Bell, Ph.D.
Vice President, Corporate Health, Safety, and Environment
Eastman Kodak Company
343 State Street
Rochester, New York 14650

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

APR 0 6 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure 12509A

Triage of 8(e) Submissions

Date sent to triage: 12/14/95

NON-CAP (CAP)

Submission number: 12509A

TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX (SEN) w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: (0) 1 2 **pages** 42 **pages** 42

Notes:

Contractor reviewer : _____ **Date:** 5/13/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0992 -12509 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: Eastman Kodak Company

SUB. DATE: 09/15/92 OTS DATE: 09/24/92 CSRAD DATE: 02/09/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0676) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME:

CAS#
538-75-0

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
(0209)	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
(0228)	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
(0248)	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:

NON-CBI INVENTORY
(YES)
NO

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)

SPECIES
GP
RBT
RAT
MUS

TOXICOLOGICAL CONCERN:
(LOW) ATOX (oral [redacted] mouse)
(MED) ATOX (inhalation, oral [redacted] rat, dermal irr/eye irr)
SEN
HIGH

USE:

PRODUCTION:
Sales: 26-180 Kg/Yr

CAS SR

[illegible]

[illegible]

12509A

M

Acute inhalation toxicity in rats is of moderate concern. Single 6-hour inhalation exposures to rats (3/dose) at levels of 159, 417, and 1320 mg/m^3 resulted in death (1/3, 3/3, and 1/3, respectively) 24-48 hours post-exposure. Clinical signs included piloerection, lacrimation, and vasodilation at all doses; in addition, dyspnea was noted at 1320 mg/m^3. At 159 mg/m^3, rats exhibited inflamed lungs. In addition, the 159-mg/m^3 that died exhibited inflammation of the trachea and stomach as well as necrosis of the stomach and liver. Mild generalized testicular atrophy was noted in one of the rats that survived this dose. At 1320 mg/m^3, rats exhibited pulmonary inflammation (3/3) and edema (2/3). One survivor at this dose had 10% of its lung consolidated and testicular atrophy.

M

Acute oral toxicity in rats is of moderate concern. Single oral gavage doses to ten rats at doses of 200-3200 mg/kg resulted in an LD_{50} of 400 mg/kg. Clinical signs included weakness, rough coat, sides caved in, and diarrhea.

L

Acute oral toxicity in mice is of low concern. Single oral gavage doses to six mice at doses of 200-800 mg/kg resulted in no deaths. Moderate weakness and rough coat were observed.

M

Dermal irritation in guinea pigs is of moderate concern. In five trials, application of the substance to guinea pig skin resulted in moderate to severe irritation. In the first trial, application of 1.0-10.0 mg/kg to the skin of two guinea pigs resulted in moderate to gross edema and erythema with hemorrhagic areas. Eschar over the entire patch area was noted at 1 week, and secondary eschar, heavy scarring, no hair or heavy black eschar were noted at two weeks. In the second trial, application of 1-10 drops to the skin of nine guinea pigs resulted in erythema, edema, and death of 8/9 animals. The surviving animals exhibited erythema or eschar covering the application area at one week and erythema with secondary eschars covering the entire area at two weeks. In the third trial, application to the skin of three guinea pigs resulted in erythema and death within 24 hours. The fourth trial involved application of 5.0-20.0 mg/kg to the skin of three guinea pigs. At 24 hours, severe to gross edema and hemorrhaging and necrosis of the patch area were noted. Moderate edema and thin eschar over the entire patch area with erythema were noted at one week, and eschars (some secondary), heavy scarring, and complete alopecia were noted at two weeks. In addition, some animals died at 3 days. The final trial involved application to the skin of one guinea pigs. Effects consisted of: severe erythema and moderate edema at 24 and 48 hours, moderate erythema at one week, and slight erythema and complete alopecia at two weeks.

M

Dermal sensitization in guinea pigs is of moderate concern. The compound was a low activity sensitizer in 2/5 guinea pigs.

M

Eye irritation in rabbits is of moderate concern. Application of several crystals to the eye of one rabbit resulted in severe irritation. Slight to moderate erythema of lids, nictitating membrane, palpebra, conjunctiva, and upper orbital conjunctiva were noted at one hour. At 24 hours, there was a slight increase of erythema and corneal staining. Moderate erythema with slight edema and injected iris were noted at 48 hours. At 14 days, the conjunctiva, cornea, and nictitating membrane were normal. The lids were thickened, perhaps from scar tissue, and there was defoliation around the eye.